Remarks

Upon entry of these amendments and remarks, claims 11, 12, 48, and 53 are cancelled. Applicants reserve the right to pursue the subject matter encompassed in the cancelled claims in future divisional or continuation applications. Claims 47 and 52 are hereby amended. Support for the amendment can be found in the application as filed. More specifically, support can be found at page 200, line 26 to page 201, line 6 of the specification. Therefore, no new matter has been added. Claims 19, 20, 24-47, 49-52, and 54-56 are now pending.

Formal matter

Claim 11 was objected to for encompassing a non-elected subject matter. *See*, Paper No. 6, page 3, second paragraph.

Applicants respectfully point out that claim 11 is hereby cancelled, thereby rendering this objection moot.

Rejection Under 35 U.S.C. § 101 and § 112

The Examiner has rejected claims 11, 12, and 25-56 under 35 U.S.C. § 101 because the invention is allegedly not supported by a credible, substantial, and specific, or well-established utility. *See,* Paper No.6, page 3, third paragraph. More particularly, the asserted utilities are allegedly not substantial because "it is not clear whether the activity is due to the direct effect of HOFND85 protein as the supernatant may contain many other molecules or factors, which may contribute to the outcome of the assay." *See*, Paper No. 6, page 4, third paragraph. It is further alleged that "the specification indicates that this protein is also expressed in normal ovarian tissue, ... , the Examiner is not able to conclude that the HOFND85 is suitable as a tumor marker[.]" *See*, Paper No. 6, page 4, fourth paragraph.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that claims 11 and 12 have been cancelled, thereby rendering their rejection under 35 U.S.C. § 101, moot. Applicants respectfully request that the rejection of claims 11 and 12 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Moreover, "an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101." M.P.E.P. § 2107.02(III)(A) at 2100-39; *see also, In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974). "Where an applicant has specifically asserted that an invention has a particular utility, the assertion cannot simply dismissed as 'wrong.'" M.P.E.P. § 2107 (III) B at 2100-40. "Office personnel should not begin by questioning the truth of the statement of utility. Instead, any inquiry must start by asking if there is any reason to question the truth of the statement of utility. This can be done by simply evaluating the logic of the statements made." M.P.E.P. § 2107.02 at 2100-39. Further, the PTO must accept the manner of making and using an invention disclosed in a specification "unless there is a reason for one of skill in the art to question the objective truth of the statement of utility or its scope." *In re Langer*, 183 U.S.P.Q. at 297; *see also, In re Marzocchi*, 58 C.C.P.A. 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) and *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1098-99 (Jan. 5, 2001). Indeed, the Federal Circuit has characterized the standard for utility by indicating:

> The threshold of utility is not high: An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. *See Brenner v. Manson*, 383 U.S. 519, 534 (1996); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992) ("To violate § 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 247, 275 (7th Cir. 1903) (the test for utility is whether the invention "is capable of serving any beneficial end").

Juicy Whip, Inc. v. Orange Bang Inc., 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999).

Accordingly, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt (*i.e.*, "question") the truth of the statement of utility. *See,* M.P.E.P. § 2107 at 2100-30; *In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995); and, *In re Cortright*, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). The Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *See id.* Such a *prima facie* showing must contain (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not specific, substantial, and credible; (2) support for factual findings relied upon in reaching this conclusion; and (3) an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. *See id.* Moreover, if applicants have presented reasoning

used in asserting a utility, the Examiner must present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the Applicants' assertion of utility. *See id.* For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

The presumption of credibility of the asserted utility accorded to Applicants should extent to the manner in which the invention was obtained. The Examiner's expressed doubt as to the effect of the HOFND85 protein implies that no, or improper, controls were used during the experimentation. The M.P.E.P. states that "in deference to applicant's understanding of his or her invention, when a statement of utility is evaluated, Office personnel should not begin by questioning the truth of the statement." *See,* M.P.E.P. 2107.02-III.A. at 2100-39. Therefore, the utility assertion by Applicants pre-supposes that the data on which it is based were significant, rendering the Examiner's argument moot.

In the instant case, Applicants have stated that the claimed protein is expressed primarily in ovarian tumor, and thus would be predictive of ovarian cancer. *See, e.g.,* specification, page 82, line 30. In addition, the specification discloses that claimed polypeptides can be used to generate antibodies which are useful, for example, as immunological probes for differential identification of ovarian cancer tissue, and in the diagnosis of ovarian cancer (*e.g.,* by tumor imaging). *See, e.g.*, specification at page 84, lines 12-14, page 264, lines 6-11, and page 269, line 31 to page 270, line 9.

Based on the above-quoted definition of a substantial utility from the M.P.E.P., Applicants have identified a material (the claimed protein) which has a stated correlation to a predisposition to the onset of a particular disease condition (ovarian cancer), thus providing a substantial utility under 35 U.S.C. § 101. Applicants point out that the M.P.E.P. states that the material need only have a stated correlation to a predisposition to a disease, not that such a correlation must be confirmed by experimentation as the Examiner suggests. Indeed, the Examiner's contention that for a diagnostic utility for cancer to be substantial requires significant further research and experimentation, such as collecting and examining large numbers of cases, and performing statistical analyses directly contradicts the warning in the M.P.E.P. against requiring such further experimentation in order to satisfy the utility requirement. Such considerations may relate to the enablement requirement, but are not relevant to whether an asserted utility is substantial under 35 U.S.C. § 101. Moreover, "the general rule [is] that the treatments of specific diseases or

conditions meet the criteria of 35 U.S.C. § 101." *See* Revised Interim Utility Guidelines Training Materials, page 6. Accordingly, the utility asserted by Applicants is clearly substantial.

In view of the foregoing, Applicants assert that one skilled in the art would more likely than not conclude that the claimed polypeptides are useful as a marker for ovarian cancer; and that antibodies generated against the claimed polypeptides could be members of a cancer marker panel to detect various forms of ovarian cancer. Further, as the Examiner has not provided evidence to rebut Applicants' substantial assertion of utility, the rejection of the claimed invention under 35 U.S.C. § 101 cannot properly be maintained. Accordingly, Applicants respectfully request that the rejection of claims 25-56 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Claims 11, 12, and 25-56 are also rejected under 35 U.S.C. § 112, first paragraph. *See*, Paper 6, page 5, second paragraph. Specifically, the Office Action asserts "since the claimed invention is not supported by a substantial or well-established utility for the reason set forth above, one skilled in the art clearly would not know how to use the claimed invention." *See,* Paper No. 6, page 5, second paragraph.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible asserted utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. Therefore, because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejections under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn. Accordingly, Applicants respectfully request that the rejection of claims 11, 12, and 25-56 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph (enablement)

The Examiner has rejected claims 11, 12, and 37-56 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. *See* Paper No.6, page 5, third paragraph. More particularly, it is stated "[t]he specification does not teach how to use any of the variants or fragments of HOFND85 polypeptide." *See*, Paper No. 6, page 4, fourth paragraph.

Preliminarily, Applicants point out that claims 11 and 12 have been cancelled, thereby rendering their rejection under 35 U.S.C. § 112, first paragraph, moot. Applicants respectfully request that the rejection of claims 11 and 12 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

To satisfy the enablement requirement, the specification must enable a person of ordinary skill in the art to practice a single use of the claimed polypeptides without undue experimentation. *See, e.g.*, MPEP §2164.01(c). To make a proper enablement rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. M.P.E.P. §2164.04; *see also, In re Wright*, 999 F.2d 1557, 1561-1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Applicants respectfully submit that the Examiner has not provided sufficient evidence or a basis to question the enablement provided in the specification for the claimed polypeptides.

The Federal Circuit has held that *making the claimed species and screening them for function is acceptable*, as long as the experimentation is not undue. As in all cases, this is the test: whether it would require undue experimentation to practice the invention – even when a claim might encompass some inoperative embodiments. *See generally, Atlas Powder v. E.I. Du Pont de Nemours & Co.* 750 F.2d 1569, 224 U.S.P.Q. (BNA) 409 (Fed. Cir. 1984). Therefore, it is clearly not *per se* undue to make and test several fragments, particularly when specific guidance was clearly disclosed in the specification coupled with what was known in the art at the time the invention was filed.

At the time the invention was filed, it was *routine* to determine empirically that particular variants of HOFND85 protein exhibit either the tissue distribution or the *antigenicity* of the parent protein. The specification describes and teaches uses of the claimed variants that do not require a retention of biological activity, for example, as an immunogen to produce antibodies against HOFND85 polypeptides, which have utility as discussed above.

Specifically, methods were available, as the priority date of the instant application, for readily making and identifying numerous altered polynucleotides and polypeptides (*see* page 191, line 18 to page 203, line 10 of the specification). These mutations could be readily generated at random, and the nucleotide and encoded amino acid sequences of the mutants could be readily determined.

In view of the above, Applicants respectfully request that the rejection of claims 25-56 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph (written description)

The Examiner has rejected claims 11, 12, and 37-56 under 35 U.S.C. § 112, first paragraph for alleged lack of written description. *See* Paper No. 6, page 6, second paragraph. More particularly, it is stated "[t]he claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity." *See*, Paper No. 6, page 6, third paragraph.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that claims 11 and 12 have been cancelled, thereby rendering their rejection under 35 U.S.C. § 112, first paragraph, moot. Applicants respectfully request that the rejection of claims 11 and 12 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Furthermore, Applicants respectfully point out that claims 37-56 do not encompass "a secreted form, a variant, an allelic variant, a species homologue, or fragments" of the polypeptides of the invention. Applicants are therefore addressing the issue of written support for the description of "% variants" as identified by the Examiner.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. The Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). While the applicant must "blaze marks on trees," rather than "simply [provide] the public with a forest of trees," an Applicant is not required to explicitly describe each of the trees in the forest. *See Unocal*, 208 F.3d at 1000. *See also* M.P.E.P. § 2163.02 ("The subject matter of the claim need not be described literally (i.e., using the same terms or in *haec verba*) in order for the disclosure to satisfy the description requirement."). The Court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as the court noted,

"the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *See In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicants respectfully submit that the Examiner has not met this burden.

Applicants respectfully disagree with the Examiner and submit that one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims in the present application as filed. Applicants further submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application. Applicants submit that the specification does, indeed, provided adequate written description to enable one of skill in the art to make useful predictions as to the positions or identities of the claimed polypeptides and to visualize or recognize the identity of the members of the genus. Specifically, the specification provides ample disclosure of relevant characteristics of the HOFND85 polypeptides. For example, the specification at page 82, lines 17-22 indicate that the polypeptides of the invention share sequence homology with the superfamily of protecadherins, which was well known at the time of filing.

Accordingly, one skilled in the art, enlightened by teachings of the present application (particularly, for example, the sequences of HOFND85), could readily envision countless polypeptide sequences that comprise the specified polypeptides. For example, the skilled artisan could clearly envision each of the polypeptides that are 95% identical to the polypeptide of SEQ ID NO:125 as a polypeptide with 1, 2, 3, 4, or up to 15 amino acid substitutions along its length. Indeed, nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides that are 95% identical to the amino acid sequence of SEQ ID NO:125. Clearly, such knowledge is well within what is expected of the skilled artisan. Further, the instant claims do not require the claimed sequences to possess any particular activity or characteristic beyond the described

sequence, and the subject matter of what is claimed is fully supported by the specification. § 112 requires no more. *See Unocal*, 208 F.3d at 1000; M.P.E.P. § 2163.02.

Therefore, Applicants assert that the specification as filed provides sufficient written description for "% variants" of the claimed polypeptides and respectfully request that the rejection of claims 37-56 be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph (enablement)

Claims 11, 12, 31-34, 42-46, and 52-56 were further rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. *See*, Paper No. 6, page 7, third paragraph. More particularly, it is stated "the specification fails to provide the deposit statement indicating the deposit material will be readily available to the public without restriction upon issuance of a patent." *See*, Paper No. 6, page 7, fourth paragraph.

Preliminarily, Applicants point out that claims 11 and 12 have been cancelled, thereby rendering their rejection under 35 U.S.C. § 112, first paragraph, moot. Applicants respectfully request that the rejection of claims 11 and 12 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

The undersigned attorney of record hereby states:

1. ATCC Deposit No. PTA-1544 containing human cDNA encoding the Secreted Protein HOFND85, clone HOFND85 was deposited with the American Type Culture Collection (ATCC), now located at 10801 University Boulevard, Manassas, VA 20110-2209, U.S.A. on March 21, 2000, in compliance with the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure.

2. I hereby assure the United States Patent and Trademark Office and the public that (a) all restrictions on the availability to the public of a sample of the above-mentioned deposited plasmid will be irrevocably removed upon issuance of a United States patent of which the plasmid(s) is a subject; (b) the above-mentioned deposited plasmids will be maintained for a period of at least five years after the most recent request for the furnishing of a sample of the plasmid was received by the ATCC and, in any case for a period of at least 30 years after the date of deposit or for the enforceable life of such patent, whichever is longer; (c) should the above-mentioned deposited plasmid become

non-viable or mutated or otherwise incapable of being furnished by the depository upon request due to the condition of the deposit, the plasmid will be replaced by the Applicants; and (d) access to the above-mentioned deposited plasmid will be available to the Commissioner during the pendency of the patent application or to one determined by the Commissioner to be entitled to such plasmid under 37 C.F.R. § 1.14 and 35 U.S.C. § 122.

Applicants assert that the above statement is sufficient to overcome the Examiner's rejection and respectfully request that the rejection of claims 31-34, 42-46, and 52-56 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 11, 12, 29, 35, 40, 45, 50, and 55 were further rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. *See*, Paper No. 6, page 8, fourth paragraph. More particularly, it is stated "claims 29, 35, 40, 45, 50, and 55 are indefinite for the recitation of 'an *acceptable* carrier' because it is unclear what it is acceptable for." *See*, Paper No. 6, page 9, fifth paragraph (emphasis original).

Preliminarily, Applicants point out that claims 11 and 12 have been cancelled, thereby rendering their rejection under 35 U.S.C. § 112, second paragraph, moot. Applicants respectfully request that the rejection of claims 11 and 12 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

Applicants further point the Examiner's attention to pages 449-460 of the specification, and more particularly to the paragraphs spanning page 451, line 29 to page 452, line 2. In that portion of the specification, a "pharmaceutically acceptable carrier" is defined, for instance, as "one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation." *See*, specification, page 451, lines 29-31. Applicants respectfully point out that it is impermissible in law to require a claim to describe the invention; this is the role of the disclosure portion of the specification, not the role of the claims. The first paragraph of 35 U.S.C. § 112 applies only to the disclosure portion of the specification, not to the claims. *See, Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1575 (1986). The full scope of the claims must be determined in light of the teachings given in the specification and Applicants assert that the instant specification provides sufficient support for the pending claims.

Applicants submit that, for the reasons stated above, claims 29, 35, 40, 45, 50, and 55 are definite in their recitation of "acceptable carrier." Accordingly, Applicants respectfully submit that the rejection of claims 29, 35, 40, 45, 50, and 55 under 35 U.S.C. § 112, second paragraph has been obviated. Applicants respectfully request that the rejection of claims 29, 35, 40, 45, 50, and 55 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 11, 47, 50-52, 55, and 56 were further rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Suzuki, WO 96/00289 (04 January 1996). *See*, Paper No. 6, page 9, eighth paragraph. More particularly, it is stated "the cited sequence anticipates claims 11, 47, and 52 as being a polypeptide at least 95% identical to a polypeptide fragment of SEQ ID NO:125 (claim 1, part (a), for example), or to a epitope of SEQ ID NO:125 (claim 1, part (d), for example), or a protein consisting of at least 30 contiguous amino acid residues of SEQ ID NO:125 (claim 47, for example) or of the complete polypeptide encoded by the HOFND85 cDNA (claim 52, for example)." *See*, Paper No. 6, page 9, ninth paragraph.

Applicants respectfully disagree.

Preliminarily, Applicants point out that claim 11 has been cancelled, thereby rendering its rejection under 35 U.S.C. § 102(b), moot. Applicants respectfully request that the rejection of claim 11 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Moreover, Applicants point out that claim 1, to which the Examiner refer in the rejection, was cancelled in response to the restriction requirement and was not examined in the present Office Action, as stated by the Examiner herself. *See*, Paper No. 6, page 2, fourth paragraph. Applicants therefore assert that the anticipation of a polypeptide at least 95% identical to a polypeptide fragment of SEQ ID NO:125 (claim 1, part (a), for example), or to a epitope of SEQ ID NO:125 (claim 1, part (d), for example) is irrelevant.

Applicants would also like to point out that claims 47 and 52 have been amended in such a way as to overcome the Examiner's rejection.

Applicants respectfully request that the rejection of claims 47, 50, 51, 55, and 56 be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 103(a)

Claims 49 and 54 were further rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Suzuki, WO 96/00289 (04 January 1996) as applied to claims 11, 47, 50-52, 55, and 56, and further in view of Capon et al. US5,116,964. *See*, Paper No. 6, page 10, fourth paragraph.

Applicants respectfully disagree and traverse. In order for a rejection under 35 U.S.C. § 103(a) to be valid, three criteria must be met (*See,* M.P.E.P. 706.02(j)):

a) there must be some suggestions or motivation to modify or to combine reference teachings;

b) there must be a reasonable expectation of success; and

c) the prior art reference (or references when combined) must teach or suggest all the claim limitations

(emphasis added).

As discussed above, Suzuki does not disclose the present invention as amended and therefore there would be no motivation or suggestion to use Suzuki's teachings, alone or in combination with any other reference, to obtain the present invention. Accordingly, Applicants respectfully request that the rejection of claims 49 and 54 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

In view of the foregoing remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. A request is made to the Examiner to call the undersigned at the phone number provided below if any further action by Applicants would expedite allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: October 3, 2003

Respectfully submitted,

By _____
Janet M. Martineau
Registration No.: 46,903
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(301) 315-2723

KKH/JMM/FR/ba